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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/926,355 | 02/19/2002 | Naoyuki Nishikawa | P21587 | 7902 |

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|---|
| SMALL, ANDREA D SOUZA |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1626 | |

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/926,355 | NISHIKAWA ET AL. | |
| | Examiner | Art Unit | |
| | Andrea D Small | 1626 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *parts of 1-3, 5 and 7-21 and claims 4, 6 and 22-29* is/are withdrawn from consideration

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 7-21* is/are rejected.

7)☒ Claim(s) *parts of 1-3, 5 and 7-21 and claims 4, 6 and 22-29* is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

***I. Preliminary Matters:***

(a) Applicants response filed 5/14/2003 has been received and entered into the file.

(b) Claims 1-29 are pending.

(c) Claim of priority under 35 USC 371 of PCT/JP00/02573, which in turn claims priority under 35 USC 119(a)-(d) to JP 11/111698 and JP 11/200228.

***II. Restriction:***

(a) Applicant's election with traverse of compound No. 5-20, example 102 dated May 15, 2003 is acknowledged. The traversal is on the ground(s) that the restriction is improper because the claims have unity of inventions as they share a common property or activity and they share a significant structural feature. This is not found persuasive because:

The criterion employed in the previous office action was whether the claims lacked unity of invention under PCT rules 13.1 and 13.2.

PCT Rule 13.1 states that the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (requirement of unity of invention).

PCT Rule 13.2 state that unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.

Annex. B, Part 1(b), provides that "special technical features" mean those technical features, which, as a whole, define a contribution over the prior art.

37 C.F.R. 1.475(e) states that the determination of whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

Upon analyzing the above cited rules, the "special technical feature" definition of Annex. B, Part I(b) may be established for alternatives within a single claim as was outlined in office action of paper no. 5. Thus the correct criterion was employed in determining whether the

claims lacked unity of invention. Further, Annex. B, Part 1, subsections (d) and (f) are illustrations of particular situations that provide examples of how lack of unity within a claim **may** be established. Further there is no requirement that any art is to be cited in order to establish that a technical feature does not provide a contribution over the art. However, attached to this office action is a copy of a reference that provides that the technical feature, which can be taken as a whole amongst all the alternatives, the indole moiety, is not a 'special technical feature' as defined in PCT Rule 13.2 by failing to define a contribution over the prior art, as it was known in the art prior to the filing of the instant application. See attached, Yuan, et al reference. Therefore, unity of invention is lacking and the lack of unity restriction as outlined in paper no. 5 is proper.

In view of the foregoing reasons, the Examiner asserts that the correct criterion was employed. However, even if the criterion to be employed is that which is outlined under 'Markush Practice', the instant claims lack unity of invention.

(f) **" Markush Practice. "** The situation involving the so-called "Markush practice " wherein a single claim defines alternatives (chemical or non-chemical) is also governed by Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B)

(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B)

(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

(ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives " refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art. The structural element may be a single component or a combination of individual components linked together.

(iii) In paragraph (f)(i)(B)(2), above, the words "recognized class of chemical compounds " mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

(iv) The fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be justification for a finding of a lack of unity of invention.

**Instantly,**

Annex. B, Part 1, (f)(i)(A): is met because Applicant has claimed that all the alternatives have a common utility. However, the unity of invention breaks down because neither of the (f)(i)(B) criteria is met.

Annex. B, Part 1, (f)(i)(B)(1): is not met because the structural element shared by all the alternatives is the indole moiety, this structural element is not a 'significant structural element' because the structural element is not distinctive in view of the existing prior art, i.e. it is not novel over the prior art. See attached Yuan, et al reference. Therefore, this criterion is not met.

Annex. B, Part 1, (f)(i)(B)(2): is not met because all the alternatives do not belong to a recognized class of chemical compounds. There is no expectation in view of the chemical arts that a substitution of each member one for the other as instantly claimed, would result in the same intended result. For example, the substitution of a phenyl at the A position results in a different class of chemical compound as the resultant compound is useful in treating CNS disorders, whereas the instant compounds are useful as treatment for diabetes, etc. See Yuan, et al.

Since the lack of unity criteria under Markush Practice is a two prong test, and since one of the prongs, (f)(i)(B)(1) or (f)(i)(B)(2), cannot be established, unity of invention is lacking and the holding of lack of unity is proper and is maintained. .

The requirement is still deemed proper and is therefore made FINAL.

(b) **The elected grouping is as follows**:

Group VI: Compound of formula I in claim 1 wherein

A is I(b);

R1, R21, R22 and R23 are as claimed in claim 1;

L is –NR3-C(O)-;

M is a bond;

X is –S-, -O-, –NR4-, -NR5-C(O)-, NR5-C(S)-, or –NR5-SO2-, or a bond wherein R4 and R5 are as claimed in claim 1; and

Y is as claimed in claim 1.

Claims readable on the elected group are claims 1-3, 5, 7-21. The remaining subject matter of claims 1-3, 5, 7-21 and claims 4, 6, and 22-29 are withdrawn from consideration as being drawn to non-elected inventions. 37 CFR 1.142(b).

***III. Rejections:***

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 19 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating some NPY diseases such as diabetes, hypercholesterolemia, hyperlipidemia or arteriosclerosis, does not reasonably provide enablement for prophylaxis (term includes prevention) for diabetes, hypercholesterolemia, hyperlipidemia or arteriosclerosis or the treatment of all NPY diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification does not give any guidance as to the treatment of NPY and prophylaxis of diabetes, hypercholesterolemia, hyperlipidemia or arteriosclerosis. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, Applicants are claiming a method of treatment of NPY diseases and prophylaxis of diabetes, hypercholesterolemia, hyperlipidemia or arteriosclerosis. The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which

compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art whether drugs that treat certain diseases would result in those diseases also being prevented. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant specification provides guidance on how to treat diabetes, hypercholesterolemia, hyperlipidemia or arteriosclerosis , in fact the specification provides assays indicating the inhibition ration of the compounds to the receptor, but has not provided assays correlating the binding assays to preventing the onset of the above named diseases by administering the instantly claimed compounds. The specification is also silent as to the ability of the compounds as instantly claimed to treat all possible diseases related to NPY. By its very definition, NPY is the most abundant neuropeptide, it potentiates not only feeding, but among other things regulates secretion of GnRH as well. The specification is silent as to how the instantly claimed compounds treat, for example, fertility disorders related to GnRH, etc. Therefore, in order to practice the claimed invention, one skilled in the art would have speculate which of the numerous compounds disclosed may present the requisite activity of prevention or treatment of all NPY associated disorders, then once the compound is determined, then the trials on various patients to determine whether administration of the compound would result in persons who have other NPY disorders could be treated or whether diabetes, hypercholesterolemia, hyperlipidemia or arteriosclerosis could be prevented. The quantity of experimentation needed would impose an undue burden on the skilled art worker. Therefore, the broad terminology treatment diseases that NPY is involved or the prophylaxis of diabetes, hypercholesterolemia, hyperlipidemia or arteriosclerosis is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 7-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 19 provides for the use of a substance, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

(b) Claims 1-3, 5, 7-21 are rejected as being unclear. These claims have parenthesis throughout the claims. It is unclear whether the subject matter in the parenthesis is part of the claimed subject matter or not. Amending the claims to delete the parenthesis is suggested to obviate the above rejections.

(c) Claims 14-17 are rejected as being indefinite as it is unclear whether Applicant is claiming a pharmaceutical composition or a method of use. Amending the claim to define the intended invention accurately is suggested to obviate the above rejection.

(d) Claims 14 and 19 are rejected to lacking antecedent basis in claim 1. Claim 19 refers to substance of claim 1. Claim 1 is drawn to a compound, therefore, claim 19 lacks antecedent basis in claim 1 from which it depends.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by (a) Brunton, et al and (b) Grammaticakis

(a) Brunton, et al discloses compounds that anticipate the instantly claimed genus where A is I(d), R1 is alkyl, R21-R23 are hydrogen, L is NHCO, M is a bond, X is O, and Yis alkyl. See RN # 101586-28-1, attached abstract.

(b) Grammaticakis discloses a compound that anticipate the instantly claimed genus where A is I(d), R1 is Acyl, R21-R23 are H, L is NHCO, M is a bond, X is NR4, where R4 is H and Y is aryl. See RN# 102659-65-4, see abstract provided.

***IV. Objections:***

(a) Parts of claims 1-3, 5 and 7-21 and claims 4, 6 and 22-29 are objected to as being drawn to non-elected inventions. 37 CFR 1.142(b).

***V. Contact Information:***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrea D. Small, whose telephone number is (703) 305-0811. The examiner can normally be reached on Monday-Thursday from 8:30 AM - 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7921. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [Joseph.McKane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive

data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1234

Andrea D. Small, Esq.
June 11, 2003

Joseph K. McKane
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